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FORM 8

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT TO APPLICATION OR REPORT
Filed Pursuant to Section 12, 13 or 15(d) of the
SECURITIES EXCHANGE ACT OF 1934

92-2243

ISIS PHARMACEUTICALS, INC.
(Exact name of registrant as specified in charter)

AMENDMENT NO. 1

The undersigned registrant hereby amends the following items, financial statements, exhibits or other portions of its Quarterly Report For The Quarter Ended March 31, 1992 on Form 10-Q as set forth in the pages attached hereto: (List all such items, financial statements, exhibits or other portions amended)

Part II: Item 6(a) Exhibits

10.3 License and Development Agreement between the Registrant and Vical Incorporated dated as of February 21, 1992 (with certain confidential information deleted)

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this amendment to be signed on its behalf by the undersigned, thereunto duly authorized, as of July 1, 1992.

ISIS PHARMACEUTICALS, INC.
(Registrant)

By: _____

Stanley T. Crooke, M.D., Ph.D.
Chairman of the Board, President and
Chief Executive Officer
(Principal Executive Officer)

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ISIS PHARMACEUTICALS, INC.
FORM 8

INDEX TO EXHIBITS

Exhibit Number	Description	Page Number
10.3	Pages 3 and 4 of License and Development Agreement between the Registrant and Vical Incorporated dated as of February 21, 1992 (with certain confidential information deleted).	4

EXHIBIT 10.3

(b) VICAL will, at its expense, use commercially reasonable efforts (taking into account the value of the Vical Patents to ISIS as well as to VICAL) to prosecute, maintain, defend and enforce the Vical Patent Applications and the Vical Patents. ISIS and VICAL shall meet as necessary to determine the scope and timing for the filing of patent applications for Vical Lipid Technology as well as the strategy for prosecuting, maintaining, defending and enforcing Vical Patents; and VICAL, based upon these discussions and in consideration of commercially reasonable principles of intellectual property protection, shall file, prosecute, maintain and defend any and all patent applications, both foreign and domestic, for Vical Patents.

(c) If VICAL decides, for any reason, not to file, prosecute, defend, maintain or enforce any Vical Patent pursuant to this Section 3.3, it will promptly notify ISIS, and ISIS may file, prosecute, defend, maintain or enforce any such Vical Patent and any costs or expenses associated with prosecuting, defending, maintaining or enforcing such Vical Patent may only be deducted from any amounts owing to VICAL hereunder. Notwithstanding the foregoing, if VICAL fails to prosecute, maintain or enforce any Vical Patent which is not a Vical Patent Application or a filing with respect thereto in the EEC, Japan or Australia, or any Vical Patent relating thereto, ISIS costs or expenses may only be deducted from royalties relating to Net Sales Revenues in the countries to which such failure relates. A failure by VICAL to file, prosecute, defend, maintain or enforce any Vical Patent pursuant to this Section 3.3 shall not be deemed a breach of this Agreement.

ARTICLE 4

PAYMENT OBLIGATIONS

4.1 License Fees.

In consideration of the licenses granted herein, ISIS will pay VICAL the following amounts:

(a) Contemporaneous with the execution of this Agreement, ISIS will pay to VICAL $500,000.

(b) On the later of:

(i) the date six months after the Effective Date or
(ii) eight weeks after delivery of the Initial Vical Deliverables as described on Exhibit B, $250,000.

(c) On the later of:

(i) the date 12 months after the Effective Date or

(ii) eight weeks after delivery of the Final Vical Deliverables as described on Exhibit B, $250,000.

Failure by ISIS to make any payment due pursuant to this Section 4.1 within 15 days after receipt of written notice, or such longer period of time during which any good faith dispute regarding such payment exists, will result in a termination of the license granted to ISIS hereunder, no amounts paid by ISIS to VICAL prior to such termination shall be refundable, and the parties shall have no future or additional obligations to each other except as to certain provisions which are stated herein to survive a termination of this Agreement.

4.2 Milestone Payments – First [ ] Licensed Products. ISIS shall provide VICAL written notice within 15 days of its becoming aware of the achievement of each of the milestone events set forth below in respect of each of the first [ ] Licensed Products developed by ISIS or its Affiliate or Sublicensee hereunder. Within 30 days after delivering each such notice, ISIS will pay to VICAL the amounts set forth below:

(a) [ ]

(b) [ ]

(c) [ ]

(d) [ ]

ISIS shall be entitled to credit [ ] of the license fee paid pursuant to Section 4.1 hereof against the first payment due pursuant to this Section 4.2. In no event shall ISIS be obligated to pay to VICAL more than an aggregate of [ ] under this Section 4.2.

4.3 Milestone Payments – Subsequent Licensed Products. ISIS shall provide VICAL written notice within 15 days of becoming aware of the NDA filing for the initial indication for the [ ] and each subsequent Licensed Product developed by ISIS or its Affiliate or Sublicensee hereunder. Within 30 days after delivery of each such notice, ISIS shall pay to VICAL [ ]